IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Linda B. Buck and Richard Axel

U.S. Serial No. : Not Yet Known

Filed : Herewith

FOR : ODORANT RECEPTORS AND USES THEREOF

1185 Avenue of the Americas New York, New York 10036

January 26, 2001

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

PRELIMINARY AMENDMENT AND INFORMATION DISCLOSURE STATEMENT

Please amend the subject application as follows:

In the claims:

Please cancel claims 25-63 without prejudice to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application.

REMARKS

Claims 1-63 were pending in the subject application. By this Amendment applicants have canceled claims 25-63 without prejudice or disclaimer. Accordingly, upon entry of this Amendment claims 1-24 will be pending.

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Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. \$1.56 and 37 C.F.R. \$1.97(a)-(b)(1), applicants would like to direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (Exhibit A).

The following references are attached hereto as Exhibits B-E:

- Araneda R.C., Kini A.D., and Firestein S. (2000) The molecular receptive range of an odorant receptor. Nature Neuroscience 3(12): 1248-1255 (Exhibit B);
- Krautwurst D., Yau K.-W., and Reed R.R. (1998)
 Identification of ligands for olfactory receptors by
 functional expression of a receptor library. Cell 95: 917926 (Exhibit C);
- Malnic B., Hirono J., Sato T., and Buck, L.B. (1999) Combinatorial receptor codes for odors. Cell 96: 713-723 (Exhibit D); and
- Zhao H., Ivic L., Otaki J.M., Hashimoto M., Mikoshiba K., and Firestein S. (1998) Functional expression of a mammalian odorant receptor. Science 279: 237-242 (Exhibit E).

The following references were previously submitted or cited in connection with the prosecution of U.S. Serial No. 08/129,079 from which the subject application claims benefit under 35 U.S.C. §120. According to 37 C.F.R. §1.98(d), copies of patents or publications that were previously cited by, or submitted to, the

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Patent Office in connection with such prior applications need not accompany the Information Disclosure Statement. Accordingly, copies of the following references are not attached to this Information Disclosure Statement:

- Anholt, R.H. (1991) Odor recognition and olfactory transduction: the new frontier. Chemical Senses 16(5):421-427.
- Buck, L. and Axel, R. (1991) A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. Cell 65: 175-187.
- Dancigier, E. et al. (1989) Olfactory marker protein gene: its structure and olfactory neuron-specific expression in transgenic mice. Proc. Nat. Acad. Sci. 86:8565-8569.
- Dhallan, R.S., Yau, K.-W., Schrader, K.A., and Reed, R.R. (1990) Primary structure and functional expression of a cyclic nucleotide-activated channel from olfactory neurons. Nature 347: 184-187.
- Fesenko, E.E. et al. (1985) Molecular mechanisms of olfactory reception. VI. Kinetic characteristics of camphor interaction with binding sites of rat olfactory epithelium. Biochimica Biophysica Acta 839(3): 268-275.
- Firestein, S. (1991) A noseful of odor receptors. Trends in Neuroscience (14)7: 270-272.
- 7. Flanagan, J.G., Lefranc, M.-P., and Rabbitts, T.H. (1984) Mechanisms of divergence and convergence of the human immunoglobulin $\alpha 1$ and $\alpha 2$ constant region gene sequences.

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Cell 36: 681-688.

- Getchell T. V. (1988) Induction of odorant-evoked current 8. transients in Xenopus oocyte injected with mRNA isolated from the mucosa of Rana pipiens. Neuroscience Letters 91(2): 217-221.
- Graziadei, P.P.C. and Graziadei M. G.A. (1979) Neurogenesis 9. and neuron regeneration in the olfactory system of mammals. I. Morphological aspects of differentiation and structural organization of the olfactory sensory neurons. Journal of Neurocytology 8(1): 1-18.
- 10. Hamm, H.E., Deretic, D., Arendt, A., Hargrove, P.A., Koenig, B., and Hofmann, K.P. (1988) Site of G protein binding to rhodopsin mapping with synthetic peptides to the α subunit. Science 241: 832-835.
- Hood, L. et al. (1985) T cell antigen receptors and the 11. immunoglobulin supergene family. Cell 40: 225-229.
- 12. Jones, D.T. and Reed, R.R. (1989) Golf: an olfactory neuron specific-G-protein involved in odorant signal transduction. Science 244: 790-795.
- 13. Julius, D. et al. (1988) Molecular characterization of a functional cDNA encoding a seritonin 1c receptor. Science 241: 558-564.
- 14. Kashiwayanagi, M. et al. (1989) High sensitivity odor sensor using artificial membrane. Kagaky Kogyo, Vol. 40, No. 11.
- 15. Lancet, D. (1986) Vertebrate olfactory reception. Ann.

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Rev. Neurosci. 9: 329-355.

- Levy, N.S. et al. (1991) Signal transduction in olfactory neurons. J. Steroid Biochem. Mol. Biol. 39: 633-637.
- 17. Maeda, N. and Smithies, O. (1986) The evolution of multigene families: Human haptoglobin genes. Ann. Rev. Genet. 20: 81-108.
- 18. Masu Y. et al. (1987) cDNA cloning of bovine substance-K receptor through oocyte expression system. Nature 329: 836-838.
- 19. Moulton, D.G. and Beidler, L.M. (1967) Structure and Function in the peripheral olfactory system. Physiol. Rev. 47: 1-52.
- Nakamura, T. and Gold, G. (1987) A cyclic nucleotide-gated conductance in olfactory receptor cilia. Nature 325: 442-444.
- Nathans, J. et al. (1986) Molecular Genetics of Human color vision: The genes encoding blue, green and red pigments; Science (1986 Apr 11) 232(4747): 193-202.
- 22. Novoselov, V.I. et al. (1987) The properties of receptor molecules from rat olfactory epithelium. Sensory Systems 1(1): 1-7.
- O'Dowd, B.F., Felkowitz, R.J., and Caron, M.G. (1989) Structure of the adrenergic and related receptors. Ann. Rev. Neurosci. 12: 67-83.

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- Pace, U. et al. (1985) Odorant-sensitive adenylate cyclase may mediate olfactory reception. Nature 316: 255-258.
- 25. Parmentier, M. et al. (1992) Expression of members of the putative olfactory receptor gene family in mammalian germ cells. Nature 355: 453-455.
- 26. Pevsner, J. et al. (1985) Isolation and characterization of an olfactory receptor protein for odorant pyrazines. Proc. Natl. Acad. Sci. USA 82: 3050-3054.
- 27. Reed, R.R. (1990) How Does the nose Know? Minireview. Cell 60: 1-2.
- 28. Rhein, L.D. and R.H. Cagan (1983) Biochemical studies of olfaction: Binding specificity of odorant to a cilia preparation from rainbow trout olfactory rosettes. J. Neurochem. 41: 569-577.
- 29. Selbie L.A. et al. (1992) Novel G protein-coupled receptors: a gene family of putative human olfactory receptor sequences. Brain Research: Molecular Brain Research 13(1-2): 159-163.
- 30. Sicard, G. (1985) Olfactory discrimination of structurally related molecules: receptor cell responses to camphoraceous odorant. Brain Res. 326: 203-212.
- 31. Sklar, P.B. et al. (1986) The odorant-sensitive adenylate cyclase of olfactory receptor cells: Differential stimulation by distinct classes of odorant. J. Biol. Chem. 261: 15538-15543.

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- Stewart, W.B. et al. (1979) Functional organization of the rat olfactory bulb analyzed by the 2-deoxyglucose method. J. Comp. Neurol. 185: 715-734.
- 33. Strader, C.D. et al. (1989) Structural basis of $\beta\text{-adrenergic}$ receptor function. FASEB J. 3: 1825-1832.
- 34. Thommesen, G. and Doving, K.B. (1977) Spatial Distribution of the EOG in the rat. A variation with odour stimulation. Acta Physiol. Scand. 99: 270-280.
- Tonegawa, S. (1983) Somatic generation of antibody diversity. Nature 302: 575-581.
- 36. Touhara, K. et al. (1991). A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. Chemtracts: Organic Chemistry, Vol. 4, No. 4. pp. 325-328.
- 37. Yoshii K. et al. (1989) Inward rectifier produced by Xenopus Oocytes injected with mRNA extracted from Carp olfactory epithelium. Synapse 3: 234-238.
- 38. European Patent Application No. 0 335 654, published October 4, 1989.
- If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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No fee, other than the enclosed fee of \$908.00 for filing this application, is deemed necessary in connection with the filing of this Preliminary Amendment and Information Disclosure Statement. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully Submitted,

John P. White

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